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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,639	06/26/2001	Randolph J. Noelle	P 0280639	9079

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,639	NOELLE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7-11,13-15,17,20,21,24-26,28-31,34,35,38-40,42,43 and 46-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7-11,13-15,17,20,21,24-26,28-31,34,35,38-40,42,43 and 46-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 3/24/06, has been entered.
Claims 1, 15, 30 and 42 have been amended

Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are under consideration in the instant application.

Claims 2-3, 5-6, 12, 16, 18-19, 22-23, 27, 32-33, 36-37, 41, 44-45 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 3/24/06.
The rejections of record can be found in the previous Office Actions.

3. Upon reconsideration of applicant's amended claims, filed 3/24/06, in conjunction with direction to page 10 of the instant specification,
the previous rejection under 35 U.S.C. § 112, first paragraph, written description / new matter has been withdrawn

4. Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50
are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are indefinite in the recitation of "a gp39 ligand" in that they only describe the molecule of interest by an arbitrary protein name. While the name itself may have some notion of the activity of the protein, there is nothing in the claims which distinctly claims the protein and variants thereof. Applicant should particularly point out and distinctly claim the "gp39 ligand" by claiming sufficient characteristics associated with the protein (e.g. CD nomenclature, activity, molecular weight, amino acid composition, N-terminal sequence, etc.). Claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly claim what that protein is and what the compositions are made up of.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

5. Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

There is insufficient written description for "a gp39 ligand" recited in the currently newly amended limitation,
"an allogeneic or xenogeneic donor cell having a gp39 ligand mediating contact dependent helper effector function with a recipient T cell".

Applicant's amendment, filed 3/24/06, provides direction to page 11, lines 6-7 and page 14, lines 30-33 of the instant specification for the amendment to the claims.

There is insufficient written description encompassing any "gp39 ligand" currently recited in the instant claims because applicant was not in possession of the relevant identifying characteristics such as structure of other physical and/or chemical characteristics of a genus of "gp39 ligands".

Appellant is relying upon certain biological activities and the disclosure of the limited representative known "CD40" at the time the invention was made (e.g., see page 2, paragraph 2 of the instant specification).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. The Court has indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The application does no more than disclose "a gp39 ligand" and the known CD40 in the Background of the instant specification and does not contain sufficient information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention.

There is insufficient written description of the claimed "gp39 ligands" broadly encompassed by the claimed invention. There is a lack of disclosure of sufficient relevant identifying characteristics coupled with a known or disclosed correlation between function and structure of the broadly diverse compounds employed in the claimed methods.

Applicant has not provided sufficient written description of a genus of "gp39 ligands that are expressed on allogeneic donor cells" other than disclosing the known expression of CD40 on such cells.

Appellant has been reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 1115).

Appellant has been directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. Also, see MPEP 2163.

6. Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lederman et al. (U.S. Patent No. 6,403,091) in view of Berschorner (U.S. Patent No. 5,597,563), Cobbold et al. (U.S. Patent No. 6,056,956), Cornaby et al. (U.S. Patent No. 4,959,302) and Sachs et al. (U.S. Patent No. 6,296,846) essentially for the reasons of record.

Applicant's arguments, filed 3/24/06, have been fully considered but are not found convincing essentially for the reasons of record set forth in the previous Office Actions.

As pointed out in the pervious Office Actions, mailed 8/31/05 and 12/29/05, applicant's arguments and the examiner's rebuttal appear to essentially the same of record.

Once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather merely asserts that the prior art does not provide sufficient suggestion or motivation to teach the administration of an "allogeneic or xenogeneic donor cells having a gp39 ligand mediating contact-dependent helper effector function with a recipient T cell" and does not address the teachings of the references individually and not their teachings individually or in combination. One cannot show non-obviousness by merely asserting that the references do not provide the sufficient elements of obviousness or by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

While applicant asserts that the teachings of Berschorner and Sachs teach presenting antigen in an environment devoid of recipient cells, the prior art does teach providing the same or nearly the same antigen presenting cells with the same or nearly the same anti-human gp39 for inducing T cell non-responsiveness to allogeneic / xenogeneic tissues and organs and does not limit the presentation in an environment devoid of recipient cells. In fact, in order to induce the non-responsive state, it is purpose of the prior art as well as the instant methods to induce the non-responsive state in recipient T cells. The use of immunosuppressive regimens in the prior art does not necessarily involve a recipient devoid of T cells.

Also, applicant's arguments concerning the key time window "from five to eight days prior to transplantation of the tissue or organ" rely upon attacking the references individually and not what would be the expected beneficial results produced from their combination.
For example, as pointed out previously; the following is noted.

As indicated in the previous Office Action, Sachs et al. was added to provide for pre-conditioning regimens for the transplant regimen to occur between days –1 and –8 (e.g. see entire document, particularly column 8, paragraph 2).

Also, it is noted that where the general conditions or a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experiments. See In re Aller,105 USPQ 233, 235 (CCPA 1955).

A particular parameter must be first recognized as a result-effective variable, a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. See In re Antoine, 195 USPQ 6 (CCPA 1977).

Here, the art recognized a fair amount of therapeutic discretion by the ordinary artisan at the time the invention was made in providing the appropriate dosing and scheduling to achieve graft survival and a tolerance permissive environment. The various times including those encompassing 5-8 days prior to transplantation for conditioning of the transplant recipient are provided in the prior art.

The rejection of record including another reference to address the pre-transplant conditioning regimen time period encompassed by the claimed methods renders the claimed methods obvious for the reasons of record.

The following is of record and provided herein for applicant's convenience.

Again, applicant argued that the prior art does not teach nor suggest the administration of tolerizing agents "from five to eight days" prior to transplantation of the tissue or organ to be transplanted, as currently amended in the instant claimed methods.

As applicant noted, Berschorner teaches the duration of an immunosuppressive such as cyclosporine can be administered from about 7 days to about 28 days prior to the infusion of tolerogenic APCs (e.g. see columns 8-9, overlapping paragraph).

Cobbold et al. teach immunosuppressive anti-T cell antibodies can be administered repeatedly from 1 – 7 days prior to exposure to tolerogenic antigen (e.g. see column 4, paragraph 3).

Cornaby et al. teach the adjustment of immunosuppressive therapy to combat rejection and that measurement of IL-2 or IL-2 receptor levels provide such information concerning impending rejection from 2 –8 days prior to a rejection episode. (e.g. see Detailed Description of the Invention, including column 9, paragraph 1-2) and that is can be helpful in appropriate scheduling of procedures associated with grafts (e.g. columns 9-10, overlapping paragraph).

The administration of tolerizing agents "from five to eight days" prior to transplantation appears well within the variable of an immunosuppressive regimen that achieved a recognized result of inhibiting or preventing graft rejection and of creating a tolerogenic environment in order to achieve long term graft survival and well within the purview of the ordinary artisan meeting the needs of the patient and desired outcome.

As pointed out previously, Cobbold et al. teach methods of preventing graft rejection in tissue and organ transplants with anti-T cell antibodies in order to induce tolerance by providing antigen (see entire document, including columns 1-4). Cobbold et al. teach the provision of the antigen and the immunosuppressant at different times to provide a tolerance-permissive environment (see column 1-4).

The ordinary artisan provided immunosuppression prior, during and after transplanting grafts of interest, including encompassing the newly amended regimen.

In addition, the prior art recognized monitoring impending rejection encompassed by the time frame of the newly amended regimen.

Further, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

As pointed out previously and in contrast to applicant's assertions and given the teachings of providing antigen and/or antigen presenting cells containing the antigen to which specific tolerance is desired, including those at the time transplant, contemporaneously with immunosuppressants, as taught by Berschorner and/or Cobbold; one of ordinary skill in the art would have been motivated to combine the immunosuppressive properties of the CD40L-specific antibodies, taught by Lederman et al., to create an environment conducive to tolerance or specific unresponsiveness in the transplantation of a number of tissues and organs at the time the invention was made.

In contrast to applicant's assertions and given the teachings of Cobbold et al. that the presence of antigen as well as the use of anti-T cell antibodies can provide an environment conducive to tolerance or specific unresponsiveness, one of ordinary skill in the art would have had a reasonable expectation of success and motivation to employ the CD40L-specific antibodies in combining antigen presenting cells in transplanting a variety of tissues and organs at the time the invention was made.

It would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Berschorner AND/OR Cobbold et al. to those of Lederman et al. to provide methods of providing an environment conducive to tolerance or specific unresponsiveness by combining an immunosuppressant such as the CD40 ligand-specific antibodies, taught by Lederman et al. with a source of alloantigen or xenoantigen, as taught by Berschorner and Cobbold et al. to transplant a variety of tissues and cells. A person of ordinary skill in the art would have been motivated to produce this resultant therapeutic regimen to provide an environment conducive to tolerance or specific unresponsiveness to decrease the rejection of the transplanted tissue or organ and to increase the survival of such transplants.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

7. Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims 1-34 of U.S. Patent No. 5,683,693,
claims 1-34 of U.S. Patent No. 5,902,585, and
claims 1-7 of U.S. Patent No. 6,375,950

for the reasons of record and further in view of Berschorner (U.S. Patent No. 5,597,563), Cobbold et al. (U.S. Patent No. 6,056,956), Cornaby et al. (U.S. Patent No. 4,959,302) and Sachs et al. (U.S. Patent No. 6,296,846) for the reasons set forth above in the rejection under 35 § USC 103(a).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims and the patented claims appear to read on the same or nearly the same methods of inducing specific unresponsiveness. Further, the patented claims appear to anticipate the instant methods.

Applicant's arguments and the examiner rebuttal are essentially the same as set forth above in the rejection under 35 § USC 103(a).

Applicant argues that the prior art does not teach nor suggest the administration of tolerizing agents "from five to eight days" prior to transplantation of the tissue or organ to be transplanted, as currently amended in the instant claimed methods.

For the reasons above, the administration of tolerizing agents "from five to eight days" prior to transplantation appears well within the variable of an immunosuppressive regimen that achieved a recognized result of inhibiting or preventing graft rejection and of creating a tolerogenic environment in order to achieve long term graft survival and well within the purview of the ordinary artisan meeting the needs of the patient and desired outcome.

It was well known and practiced by the ordinary artisan to provide immunosuppression prior, during and after transplanting grafts of interest, including encompassing the newly amended regimen.

In addition, the prior art recognized monitoring impending rejection encompassed by the time frame of the newly amended regimen

Also, the instant claims would anticipate the patented claims.

Applicant's arguments have not been found persuasive.

Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are directed to an invention not patentably distinct from claims 1-34 of commonly assigned U.S. Patent No. 5,683,693 and claims 1-34 of commonly assigned U.S. Patent No. 5,902,585 and further in view of Berschorner (U.S. Patent No. 5,597,563), Cobbold et al. (U.S. Patent No. 6,056,956), Cornaby et al. (U.S. Patent No. 4,959,302) and Sachs et al. (U.S. Patent No. 6,296,846) for the reasons set forth above in the rejection under 35 § USC 103(a).

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 5,683,693 and U.S. Patent No. 5,902,585, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Agaion, it is noted that applicant's previous amendment indicates that terminal disclaimer will be filed upon clarification of the inventorship and ownership.

8. No claim allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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